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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,800	09/23/2003	Richard M. Weinshilboum	07039-118003	2185

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/668,800	WEINSHILBOUM ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18 and 32-47* is/are pending in the application.

4a) Of the above claim(s) *35-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-17 and 19-31 have been canceled. Claims 18 and 32-47 are at issue and are present for examination.

Applicant's election without traverse of Group I, drawn to methods for determining the sulfonator status of a subject comprising detecting the presence or absence of a *SULT1A1* allozyme (claims 18 and 32-24) in the reply filed on 4/21/06 is acknowledged.

Claims 35-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/21/06.

Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33 is unclear in the recitation of "having an adenine residue at nucleotide 638" as it is unclear as to what sequence is being referenced.

Claims 18 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for determining the ability of a human subject to transfer a sulfate group to p-nitrophenol by detecting the presence or absence of a

SULT1A1 allozyme encoded by a nucleic acid having an adenine residue at nucleotide 638 or a *SULT1A1*2* allozyme, does not reasonably provide enablement for determining the ability of a subject to transfer a sulfate group to any substrate in a subject by detecting the presence or absence of any sulfotransferase allozyme in said subject, a *SULT1A1, SULT1A2 or SULT1A3* allozyme, a *SULT1A1* allozyme encoded by a nucleic acid having an adenine residue at nucleotide 638 or a *SULT1A1*2* allozyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 18 and 32-34 recite methods for determining the sulfonator status in a subject by detecting the presence or absence of any sulfotransferase allozyme in said subject (Claim 18), a *SULT1A1, SULT1A2 or SULT1A3* allozyme (Claim 32), a *SULT1A1* allozyme encoded by a nucleic acid having an adenine residue at nucleotide 638 (Claim 33) or a *SULT1A1*2* allozyme (Claim 34). Sulfonator status is defined in the specification as the ability of a subject to transfer a sulfate group to a substrate. The specification and art each disclose that a variety of sulfotransferases sulfonate a wide variety of organic compounds, that a number of sulfotransferases are expressed in

mammalian cells of which the encoding genes for many have been cloned, and that a number of polymorphisms of many of these genes exist. However, to determine the ability of a subject to transfer a sulfate group to any substrate from the presence or absence of a particular polymorphism requires a clear knowledge of an established correlation between the presence/absence of a specific allele associated with the site detected and the ability of a subject to transfer a sulfate group to a particular substrate. Such correlations are very difficult to establish in view of the extremely complex nature of the art. A wide variety of factors effect the ability of a subject to transfer a sulfate group to a particular substrate and these may be different for every potential substrate of interest. While sulfotransferases are clearly important enzymes in the bioactivity of many organic compounds, the effects of sulfonation may increase the activity or toxicity of some compounds and decrease the activity or toxicity of others. Furthermore, the alteration in the structure/activity of any particular sulfotransferase for any particular allozyme (such as *SULT1A1*2*) may differentially effect its ability to act on different substrates, i.e., might increase the ability to sulfonate one substrate while simultaneously decreasing the ability to sulfonate other substrates as different substrates will fit into the substrate binding pocket

of the enzyme differently and will be differently affected by particular changes in the substrate binding pocket. Furthermore, there are a large number of different sulfotransferase genes which are differently expressed in distinct tissue types and have sometimes overlapping and sometimes distinct substrate specificities such that a showing that *in vitro* or in one tissue/cell type the expression of one allozyme correlates to an increased/decreased ability to sulfonate a particular compound might not be predictive of the ability to sulfonate the same substrate *in vivo* or in different tissues depending of whether other sulfotransferases catalyzing the same reaction are present or absent in each of those tissues.

The specification teaches only that the *SULT1A1*2* allozyme as a lower ability to sulfonate p-nitrophenol in human platelet and liver samples. The specification in fact discloses that most other sulfotransferase allozymes lack any difference in activity of the sulfotransferase to sulfonate p-nitrophenol and has no data with regard to any other substrates. Determining a correlation between any allozyme of *SULT1A1* or of any sulfotransferase and the ability to sulfonate any other substrate would be require undue experimentation as there is not even any showing of difference in activity of the encoded enzyme

with any substrate and applicants claims in fact encompass even the use of genes for which they have not disclosed **any** polymorphisms (i.e., they are not limited to phenol sulfotransferase gene polymorphisms). As such it would require undue experimentation for one to determining the sulfonator status in a subject by detecting the presence or absence of by determining the presence or absence of any sulfotransferase allozyme (or even the presence or absence of the SULT1A1*2 allozyme) in said subject.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18 and 32-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Raftogianis et al. (Reference AAA of applicants IDS of 2/5/04)

Raftogianis et al. teach methods of determining the presence or absence of a *SULT1A1*2* allozyme by detecting the presence of an adenine residue at nucleotide 638 of a *SULT1A1* encoding nucleic acid in human subjects. Raftogianis et al.

further teach that the *SULT1A1*2* allozyme has lower sulfotransferase activity to sulfonate p-nitrophenol.

Claims 18, 32 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Raftogianis et al. (Reference AY of applicants IDS of 2/5/04)

Raftogianis et al. teach methods of determining the activity of the STP1 sulfotransferase (*SULT1A1*) of human subjects by the presence or absence of a *SULT1A1*2* allele. Raftogianis disclose that there is a significant correlation between the TS PST phenotype (i.e., high/low activity) and the STP1 genotype for the two common STP1 alleles (i.e., *SULT1A1*1* and *SULT1A1*2*).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1600~~ 1652